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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,366	01/18/2001	Jennifer L. Hillman	PF-0293-3 DIV	1889

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EXAMINER	
ROARK, JESSICA H	

ART UNIT	PAPER NUMBER
1644	11

DATE MAILED: 10/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/766,366	HILLMAN ET AL.	
	Examiner	Art Unit	
	Jessica H. Roark	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10,11,22 and 24-39* is/are pending in the application.

4a) Of the above claim(s) *1,11,22,24,27,29,38 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,25,26,28 and 30-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. *Claims* 1, 10-11, 22 and 24-39 *are pending.*

2. Applicant's election with traverse of Group II (claims 10, 25-26, 28 and 30-37) in Paper No. 10 is acknowledged.

The traversal is on the grounds that the search of all groups overlap, and that claims substantially corresponding to the instant claims but differing in scope have already been allowed in ancestor applications. Applicant concludes that the search burden on the Examiner to examine all groups would therefore be minimal. This is not found convincing for the reasons of record set forth in Paper No. 8 at section 11, in particular with respect to the recognized divergent subject matter of the different groups and their different classification.

Applicant further traverses on the grounds that the method claims of Groups IV-VI should be rejoined to claims of Group II as per In re Ochiai and In re Brouwer. Rejoinder of process claims to an allowable product claim is appropriate only once an allowable product claim has been identified. *Until an allowable product claim is identified*, claims to the non-elected invention are withdrawn from further consideration under 37 CFR 1.142.

In view of the rejections set forth below, the issue of rejoinder of claims 24, 27, 29 and 38-39 is held in abeyance.

Claims 1, 11, 22, 24, 27, 29 and 38-39 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 10, 25-26, 28 and 30-37 *are under consideration in the instant application.*

3. Sequence compliance: The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

4. The reference to earlier filed application 09/265,294 in the first line of the specification should be updated to indicate "now Patent No. 6,210,890" following the filing date of the parent application.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

It is suggested that Applicant amend the Title to read:
-- ANTIBODIES TO A HUMAN PEROXISOMAL THIOESTERASE --

6. The formal drawings submitted 1/18/01 have been approved by the Draftsman.

7. Applicant's IDS, filed 1/18/01 (Paper No. 7), is acknowledged.

8. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

9. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 C.F.R. § 1.75(d)(1) and M.P.E.P. § 608.01(l). Correction of the following is required:

> There does not appear to be clear antecedent basis for each of the individual method steps of claims 30 and 33; and therefore for the products of claims 31-32 and 34-35 produced by the methods of claims 30 and 33. Applicant is requested to identify support in the instant specification for each method step, particularly step "b" of claim 30 and steps "b", "c" and "e" of claim 33.

10. Claim 28 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form.

The definition of an "antibody" provided on page 7 of the specification does not appear to encompass labeled antibodies. Thus an antibody that is labeled is broader in scope than the antibody in the composition of claim 26.

11. Claims 10, 25-26, 28 and 30-37 are objected to as either directly or indirectly depending from non-elected claim 1.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

13. Claims 10, 25-26, 28 and 30-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies or fragments thereof which specifically bind SEQ ID NO:1, does not reasonably provide enablement for antibodies or fragments thereof which specifically bind an isolated polypeptide *comprising* various fragments or naturally occurring "variants" of SEQ ID NO:1, as set forth in instant claim 1 from which claim 10 depends. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has disclosed antibodies to the polypeptide of SEQ ID NO:1, which is a peroxisomal thioesterase. The specification discloses that the polypeptide of SEQ ID NO:1 is involved fatty acid metabolism, an activity also supported by the teachings of Jones et al. (J. Biol. Chem. 1999; 274(14):9216-9223). The specification further discloses that antibodies to the polypeptide of SEQ ID NO:1 may be used for detecting (e.g., page 24) and purifying (e.g., page 51) the polypeptide of SEQ ID NO:1.

The instant claims are drawn to an extensive genus of antibodies to "isolated polypeptides *comprising*" various fragments or amino acid sequences having at least 90% sequence identity to SEQ ID NO:1. It is noted that the antibodies as recited do not specifically bind discrete peptide subsequences of SEQ ID NO:1 (claims 1a, c and d) or even a full length variant of SEQ ID NO:1 having a mutation in 10 out of every 100 amino acid residues (claim 1b). Instead, the claims are drawn to antibodies to isolated "polypeptides comprising" these sequences.

The phrases "an amino acid sequence of SEQ ID NO:1" in claim 1a and an "immunogenic fragment" in claim 1d read on a multitude of subsequences of SEQ ID NO:1 present in the context of an isolated polypeptide otherwise structurally and functionally unrelated to the polypeptide of SEQ ID NO:1. Similarly, "a biologically-active fragment" of the amino acid sequence of SEQ ID NO:1, as recited in claim 1c, can be any subsequence of SEQ ID NO:1 which can be characterized in any assay as having any "biological activity". Such a general recitation does not provide the skilled artisan with sufficient guidance as to which particular testable biological activity is shared between SEQ ID NO:1 and an isolated polypeptide comprising a subsequence of SEQ ID NO:1. Neither is their any requirement that the "biological activity" be enzymatic activity.

Thus although in each case some fragmentary sequence of SEQ ID NO:1 is shared by SEQ ID NO:1 and the "isolated polypeptide comprising" the fragment, there is no requirement that the isolated polypeptide of the preamble and the polypeptide of SEQ ID NO:1 share any particular function, or even that they share a structure beyond that defined by the shared fragment, which may be only a minimal portion of the total structure.

Similarly, the antibodies of the instant can bind "variant" polypeptides rather than the polypeptide of SEQ ID NO:1. Although "naturally-occurring" and having 90% sequence identity to SEQ ID NO:1, these "variant" polypeptides nevertheless do not necessarily share any testable function with the polypeptide of SEQ ID NO:1. Since the skilled artisan has not been given sufficient guidance as to how to use such variant polypeptides which do not necessarily share the enzyme activity of the polypeptide of SEQ ID NO:1; the skilled artisan has also not been give sufficient guidance as to how to use antibodies to such "variant" polypeptides.

In addition, the specification fails to provide sufficient guidance as to the antibody epitopes in SEQ ID NO:1, either linear or conformational, that results in antibodies that bind the polypeptide of SEQ ID NO:1. Definition of the epitope(s) of a particular polypeptide recognized by an antibody is essential to both make and use an antibody to fragments of the polypeptide of interest when the fragment is contained within larger polypeptide sequences. Abaza et al. (Journal of Protein Chemistry, Vol. 11, No. 5, 1992, pages 433-444) teaches single amino acid substitutions **outside** the antigenic site on a protein effect antibody binding; thus it is also essential to provide some guidance as to the identity of the flanking sequences of a fragment of a polypeptide of interest. Further, Li et al. (Proc. Natl. Acad. Sci. USA 77: 3211-3214, 1980) disclose that dissociation of immunoreactive from other biological activities when constructing analogs (see entire document).

Thus in the absence of guidance to a particular epitope and the structural context in which the epitope is found; it is highly unpredictable which other isolated polypeptides comprising a subsequence of SEQ ID NO:1 would maintain the relevant antibody epitope(s).

The disclosed enabled uses of antibodies in the specification as filed appear to require that the antibody bind the polypeptide of SEQ ID NO:1 or a polypeptide which shares both enzymatic activity and antibody epitopes with the polypeptide of SEQ ID NO:1. Given that the disclosure does not appear to identify the epitope, either linear or conformational, that must be present in a polypeptide before an antibody can be produced that bind the polypeptide of SEQ ID NO:1; there is insufficient guidance either as to how to make antibodies to the isolated polypeptide comprising some fragment of SEQ ID NO:1 for which no guidance is given as to the nature of the remaining structure (i.e., the structure of the polypeptide "comprising"); or as to how to use antibodies which binds to polypeptides which share a subsequence of SEQ ID NO:1 or are a variant of SEQ ID NO:1, but that do not bind SEQ ID NO:1 itself.

The scope of the claimed antibodies is not commensurate with the enablement provided by the disclosure with regard to the various isolated polypeptides comprising subsequences as broadly encompassed by the claimed invention. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without further guidance as to the nature of the antibody epitope in the context of a "polypeptide comprising" various subsequences or sequence variants of SEQ ID NO:1; it is unpredictable which "polypeptides comprising" would still elicit antibodies which also bound the polypeptide of SEQ ID NO:1. Consequently, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

14. Claims 10, 25-26, 28 and 30-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification appears to provide an adequate written description of antibodies to the polypeptide of SEQ ID NO:1, and for antibodies to a fragment of SEQ ID NO:1, wherein the antibodies also bind the polypeptide of SEQ ID NO:1.

However, the instant claims are drawn to an extensive genus of antibodies to "isolated polypeptides *comprising*" various fragments or amino acid sequences having at least 90% sequence identity to SEQ ID NO:1. The antibodies as recited do not specifically bind discrete peptide subsequences of SEQ ID NO:1 (claims 1a, c and d) or even a full length variant of SEQ ID NO:1 having a mutation in 10 out of every 100 amino acid residues (claim 1b). Instead, the claims are drawn to antibodies to isolated "polypeptides comprising" these sequences.

Thus the instant claims encompass antibodies which bind sequences unrelated to SEQ ID NO:1, so long as some fragment, or even a fragment having at least 90% identity to SEQ ID NO:1, is contained with the isolated polypeptide bound by the antibody. The instant claims are therefore drawn to an extensive genus of antibodies to proteins having highly diverse structures and functions for which Applicant does not appear to have provided a representative number of species. Neither do the instant claims provide for a correlation between a particular structure and a testable function specific to that structure.

Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of polypeptide sequences may be achieved by means of a recitation of a representative number of antibodies which specifically bind a representative number of "polypeptides comprising" falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. See Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

15. Applicant is reminded that affidavits and declarations, such as those under 37 CFR 1.131 and 37 CFR 1.132, filed during prosecution of the parent application do not automatically become a part of this application. Where it is desired to rely on an earlier filed affidavit, the applicant should make the remarks of record in the later application and include a copy of the original affidavit filed in the parent application.

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

17. Claims 10, 26, 28 and 30-32 are rejected under 35 U.S.C. 102(a) as being anticipated by Liu et al. (J. Biol. Chem. May 23, 1997; 272(21):13779-13785, see entire document), as evidenced by the attached alignment of SEQ ID NO:1 and SWISS-PROT accession # O14734.

Liu et al. teach the cloning and characterization of the thioesterase hTE, a protein found to interact with the HIV-1 Nef protein (see entire document, especially Fig. 2 and discussion). As evidenced by the attached alignment, residues 19-319 of hTE are identical to residues 11-311 of the instant polypeptide of SEQ ID NO:1. In addition the query match between the polypeptide of SEQ ID NO:1 and hTE is 97.3%.

Liu et al. also teach the production of a polyclonal antibody to the hTE protein produced by immunizing rabbits with a fragment of hTE from Q304 to K318 (i.e., the peptide QEGVIRVKPQVSESK); the affinity purification of the antisera on hTE; and the formulation of the antisera in a composition comprising an acceptable excipient/suitable carrier (Tris neutralized glycine HCl) (see e.g., page 13780 "Co-immunoprecipitation Experiments in CEM Cells Expressing HIV-1 NefLai" and Figure 2). It is also noted that an antisera is itself is a composition comprising an antibody and an acceptable excipient.

Since the antisera of Liu et al. specifically binds a protein identical to instant SEQ ID NO:1 from residue 11-311, the antisera that specifically binds hTE meets the limitations of an isolated antibody which specifically binds an isolated polypeptide comprising an amino acid sequence that is

an amino acid sequence of SEQ ID NO:1 (i.e., a fragment of SEQ ID NO:1 is contained within hTE);
a naturally-occurring amino acid sequence having at least 90% sequence identity to SEQ ID NO:1 (i.e., hTE); and
an immunogenic fragment of SEQ ID NO:1 (i.e., the immunizing peptide of hTE).

In addition, hTE is inherently a polypeptide comprising a biologically-active fragment of SEQ ID NO:1, particularly since Liu et al. establish that hTE has thioesterase activity (see e.g., page 13781).

Liu et al. further teach using the antisera to detect hTE associated with Nef in western blots (e.g., Figure 4). The Materials and Methods associated with Figure 4 (e.g., page 13780, "Co-immunoprecipitation Experiments in CEM Cells Expressing HIV-1 NefLai") further teach detection of the anti-hTE antibody using an enhanced chemiluminescence system. Thus Liu et al. also teach a composition comprising the antibody wherein the antibody is labeled, since the anti-hTE and label of the chemiluminescence system are also a composition, and the chemiluminescence system acts as a "label" for the anti-hTE antibody.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the anti-hTE antibody of Liu et al.

The reference teachings thus anticipate the instant claimed invention.

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

19. It is noted that although certain broad claims are anticipated by the teachings of the references, these claims have also been included in the following rejections under 35 USC 103(a) in order to address the scope of the claims.

20. Claims 10, 26, 28 and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (J. Biol. Chem. May 23, 1997; 272(21):13779-13785 in view of Zola (Monoclonal Antibodies: A Manual of Techniques, CRC Press, Boca Raton, Florida 1987, "Introduction" pages 1-11).

The claims are drawn to a monoclonal antibody to a polypeptide comprising an amino acid sequence of SEQ ID NO:1, methods of making and compositions comprising said antibody.

Liu et al. have been discussed supra and teach polyclonal antibodies to the hTE polypeptide which is identical to the instant polypeptide of SEQ ID NO:1 from residue 11-311, and use of the antibodies to detect hTE.

Liu et al. do not teach monoclonal antibodies to a polypeptide comprising an amino acid sequence of SEQ ID NO:1, methods of making and compositions comprising said antibody.

Zola teaches production of monoclonal antibodies using techniques well known in the art at the time the invention was made (e.g., see "Title"). Zola compares in Chapter 1 monoclonal antibodies and polyclonal antibodies (antisera). Zola concludes that monoclonal antibodies are advantageous over conventional antisera when the two antibody sources are compared, and further that monoclonal antibodies can be used in situations where polyclonal antisera would not even be considered (page 9, 3rd paragraph). In particular Zola notes that monoclonal antibodies provide both an opportunity for standardization and an unlimited source of reagent versus a polyclonal antisera (page 9 "V. Monoclonal Antibodies as Standard reagents").

In particular, Zola teaches immunizing an animal with an antigen of interest, isolating antibody producing cells from the animal, fusing the antibody producing cells with immortalized cells, culturing the resulting hybridoma cells, and isolating from the culture monoclonal antibody which binds the antigen of interest (summarized in Figure 4 on page 5).

Therefore, it would have been obvious to the ordinary artisan to prepare an anti-hTE monoclonal antibody using the basic immunization strategies taught by Liu et al., or using the full length hTE polypeptide. The ordinary artisan would have been motivated to produce a monoclonal antibody to hTE to replace the polyclonal antisera of Liu et al. because; as taught by Zola, the ordinary artisan would have expected that, among other advantages, a monoclonal antibody would provide an indefinite and easily obtainable supply of antibody (as opposed to antisera). In addition, the ordinary artisan would have been motivated to provide the monoclonal antibodies in suitable carriers such as saline or Tris buffered glycine for use in the detection methods taught by Liu et al., or for other applications involving the monoclonal antibody, since placing antibodies in pharmaceutically acceptable carriers was well known in the art at the time the invention was made. Similarly, the ordinary artisan would have been motivated to label the monoclonal antibody for use in the detection method of Liu et al. in replacement of the polyclonal antisera.

Given the teachings of Liu et al. with respect to the antigen in view of the art-recognized methodology as taught by Zola; the ordinary artisan would have had a reasonable expectation of producing a monoclonal antibody which, like the polyclonal antisera taught by Liu et al. would specifically bind the hTE polypeptide, which is identical to instant SEQ ID NO:1 from residue 11-311. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

21. Claims 25 and 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (J. Biol. Chem. May 23, 1997; 272(21):13779-13785 in view of Zola (Monoclonal Antibodies: A Manual of Techniques, CRC Press, Boca Raton, Florida 1987, "Introduction" pages 1-11),
as applied to claims 10, 26, 28 and 33-35 above;
and further in view of Ramakrishnan et al. (US Pat. No. 5,817,310).

The claims are drawn to various forms of an antibody and methods of making antibodies by screening recombinant immunoglobulin and Fab expression libraries.

Liu et al. each in view of Zola have been discussed supra and teach a monoclonal antibody to a polypeptide comprising an amino acid sequence of SEQ ID NO:1, methods of making and compositions comprising said antibody.

Liu et al. each in view of Zola differ by not teaching chimeric, single chain, humanized or Fab/$F(ab')_2$ fragments of the antibody, nor by teaching that such antibodies can be isolated from Fab expression and recombinant immunoglobulin libraries.

However, one of ordinary skill in the art at the time the invention was made recognized that there were many ways to produce an antibody, and that the various forms of antibody were art-recognized variants of one another.

For example, Ramakrishnan et al. teach that the ordinary artisan at the time the invention was made recognized that antibodies could be formulated in any of a variety of interchangeable forms for use as compositions comprising a pharmaceutically acceptable carrier in a variety of art recognized assays to detect a protein of interest (see entire document, especially columns 8-17). Ramakrishnan et al. teach that antibodies can be single chain antibodies, Fab fragments, or $F(ab')_2$ fragments (see e.g. column 9 at lines 9-27), as well as chimeric antibodies (e.g., column 14). Ramakrishnan et al. also teach that it was well known in the art that antibodies to a protein of interest could produced by screening a recombinant immunoglobulin library which encode either the antibodies or fragments thereof (i.e. Fab) (e.g., see column 12 at line 56 to column 13). Further, compositions comprising antibodies in a pharmaceutically acceptable carrier, and various art recognized applications of antibodies for detection are taught in columns 15-17. Labeling of antibodies for use in various applications is also taught (e.g., column 11).

Therefore, it would have been obvious to the ordinary artisan at the time the invention was made to prepare antibodies in any of the instantly recited forms for use in art-recognized assays such as those of western blotting as taught by Liu et al. The ordinary artisan would have been motivated to make these various forms of antibodies in view of the art-recognized interchangeability of the different antibody forms and in order to provide a variety of detection reagents that could be used in detection assays such as the western blotting assay taught by Liu et al. The ordinary artisan recognized the advantage of antibody variants for use in such detection assays because depending upon the other antibodies used in combination, the antibody variants could be labeled using differential secondary reagents, thus avoiding high backgrounds in immunofluorescence and immunoblotting assays. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

22. No claim is allowed.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica H. Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday, 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
October 9, 2002

Phillip Gambel
PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
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10/10/02